2-Amino-8-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one: Synthesis and Conformation of a 5-Aza-7-deazaguanine Fluoronucleoside

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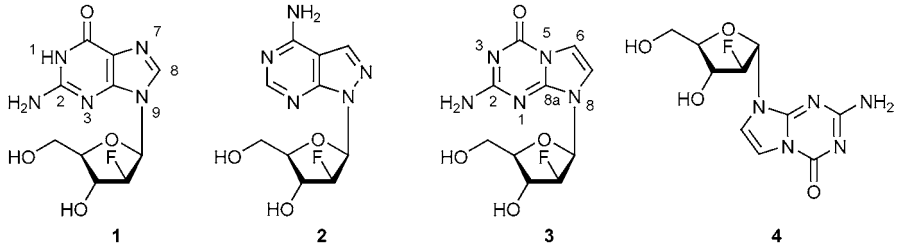
Nucleobase-anion glycosylation of 2-[(2-methyl-1-oxopropyl)amino]imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one (**6**) with 3,5-di-*O*-benzoyl-2-deoxy-2-fluoro-α-D-arabinofuranosyl bromide (**8**) furnishes a mixture of the benzoyl-protected anomeric 2-amino-8-(2-deoxy-2-fluoro-D-arabinofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-ones **9**/**10** in a ratio of *ca.* 1:1. After deprotection, the inseparable anomeric mixture **3**/**4** was silylated. The obtained 5-*O*-[(1,1-dimethylethyl)diphenylsilyl] derivatives **11** and **12** were separated and desilylated affording the nucleoside **3** and its α-D anomer **4**. Similar to 2′-deoxy-2′-fluoroarabinoguanosine, the conformation of the sugar moiety is shifted from *S* towards *N* by the fluoro substituent in *arabino* configuration.

Introduction. – Naturally occurring organohalogen compounds are abundant in plants, microorganisms, and fungi [1]. However, only 13 F-containing natural products have been isolated. Their structures cover relatively simple molecules such as fluoroacetate, which was already found in 1943 [2], and more-complicated molecules such as the nucleoside nucleocidin [3]. Recently, 5-fluorouracil derivatives were detected in sponge [4].

It has been reported that an F-substituent strongly affects the chemical, physical, and biological properties of molecules [5]. F-Substitution at nucleosides can enhance biological activity and increase chemical or metabolic stability [6–8]. Owing to the small *Van der Waals* radius of the F-substituent that is comparable with that of a H-atom, the presence of an F-atom in a nucleoside does not lead to significant steric perturbations of the shape of the molecule. Thus, fluorinated nucleosides are isosteric to their natural counterparts. At the same time, the F-atom is the substituent with the highest electronegativity. Its incorporation gives rise to essential changes of the electronic properties of a heterocyclic base and/or the conformational behavior of the pentofuranose ring and, as a consequence, to changes of the biochemical properties of the modified nucleosides. Thus, C(2) fluorination of adenosine residues renders these analogues resistant towards deamination by adenosine deaminase (ADA) [8]. The 2′-deoxy-2′-fluoroguanosine, which may be considered as an analogue of guanosine and simultaneously of 2′-deoxyguanosine, shows high anti-influenza-virus activity as well as a higher metabolic stability regarding cleavage by purine nucleoside phosphorylase (PNP) [9].

Previously, several purine nucleosides containing the 2-deoxy-2-fluoro-β-D-arabinofuranosyl moieties such as the 2′-deoxyguanosine derivative **1** have been synthesized

[10]. These compounds have the potential to act as antiviral and antileukemic agents [9][11][12]. More recently, the synthesis of 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-amine (**2**) has been reported, which shows activity against human cytomegalovirus and hepatitis-B virus, as well as against herpes-simplex virus [13].

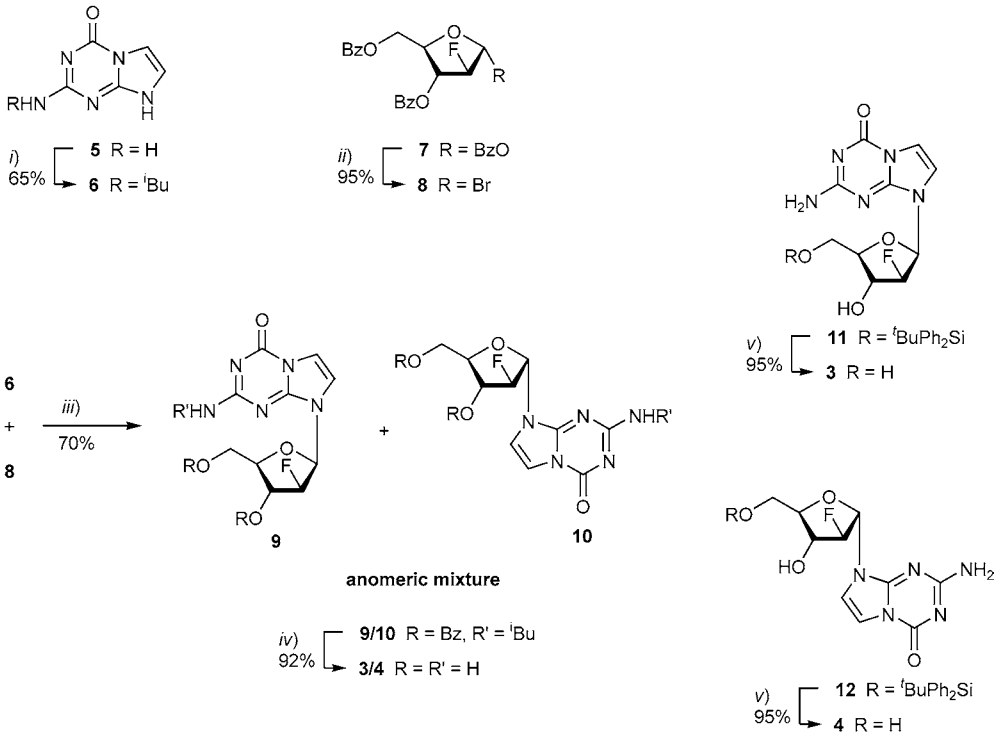


In nucleosides the most populated conformations of the furanose ring are North (*N*; C(3′)-*endo*) and South (*S*; C(2′)-*endo*). These conformations are dependent of various *gauche* and anomeric effects [14]. In 2′-deoxyribonucleosides, the 5′-OH and the 3′-OH groups prefer a *gauche* orientation resulting in an *S*-sugar pucker. In the case of 2′-deoxy-2′-fluoro-β-D-arabinonucleosides containing a modified nucleobase, the situation is more complex depending on the strong *gauche* effect of the highly electronegative F-atom and on the anomeric-effect influences of the modified base [15][16]. In continuation of our studies performed on pyrazolo[3,4-*d*]pyrimidine 2′-deoxy-2′-fluoro-D-arabinofuranonucleosides, we report on the synthesis and conformational properties of the of 2-aminoimidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one nucleosides **3** and **4** containing the sugar moiety with the F-substituents in the 2′-'up' position (*arabino* configuration).

Results and Discussion. – *Synthesis.* Various synthetic routes have been developed to prepare 2′-deoxy-2′-fluoro-β-D-arabinofuranonucleosides [17][18]. The synthesis of the target molecules **3** and **4** was performed in a convergent way as it has been reported for the fluorinated nucleoside **2** [8]. Before glycosylation, 2-aminoimidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one (**5**) was protected at the 2-amino group with an isobutyryl residue ($\rightarrow$**6**) [19] (*Scheme*). The condensation of **6** with the fluoroglycosyl bromide **8** was then performed under the conditions of nucleobase-anion glycosylation in MeCN in the presence of K_2CO_3 or DBU as base [13][20]. For this purpose, commercially available 1,3,5-tri-*O*-benzoyl-2-deoxy-2-fluoro-α-D-arabinofuranose (**7**) was readily transformed to 3,5-di-*O*-benzoyl-2-deoxy-2-fluoro-α-D-arabinofuranosyl bromide (**8**) [21]. The glycosylation of **6** [19] with the fluoroglycosyl bromide **8** was finally carried out in MeCN, with TDA-1 (tris[2-(2-methoxyethoxy)ethyl]amine) as a catalyst and potassium carbonate as base. Compared to the glycosylation reaction of the same base with the 2-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl chloride [19], the reaction was prolonged (24 h). As a partial deprotection of the benzoyl group was observed, the reaction mixture was directly treated with ammonia-saturated MeOH to give an anomeric-nucleoside mixture **3**/**4** in 55% yield. However, application of the recently

suggested DBU salt glycosylation [13] for the same condensation of **6** with **8** gave also an anomer mixture of protected nucleosides **9**/**10**, but in higher yield (70%). At this stage, the ^{1}H-NMR spectra and HPLC profiles displayed a *ca.* 1:1 ratio (α/β-D) of the anomeric nucleosides (data not shown).

Scheme



i) Isobutyric anhydride, H_3PO_4, reflux, 1 h, 65%. *ii*) 30% HBr soln./AcOH, CH_2Cl_2, 18 h; r.t.; 95%. *iii*) DBU, MeCN, Ar, 24 h, r.t.; 70%. *iv*) NH_3 (g) in MeOH, 24 h, r.t.; 92%. *v*) Bu_4NF, THF, 0.5 h, r.t.; 95%.

The formation of the anomeric-nucleoside mixture obtained during nucleobase-anion glycosylation differs from the outcome of the reaction products of other nucleobases. In most other cases, a stereoselective reaction is observed when the fluoro-β-D-glycosyl bromide **8** is employed [22]. This was verified with pyrazolo[3,4-*d*]pyrimidines as well as with pyrimidine nucleosides [18]. As the nucleobase **6** yields also anomer mixtures when the stereochemically pure 2-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl chloride is employed, the formation of anomer mixtures is the result of the particular properties of the protected nucleobase **6**. The anomer mixture of the fluoronucleosides **9**/**10** was separable by anal. HPLC, but not on a preparative scale by silica-gel column chromatography. Thus, deprotection with ammonia-saturated MeOH was performed as described [23] resulting again in an inseparable mixture of the free nucleosides **3**/**4** (92% yield). To accomplish separation, the mixture **3**/**4** was transiently protected with the (*tert*-butyl)diphenylsilyl residue by

treatment with (*tert*-butyl)chlorodiphenylsilane/1*H*-imidazole at room temperature. The obtained anomer mixture **11**/**12** of the 5′-*O*-silylated compounds was now separable by column chromatography, and the individual anomers **11** (β-D) and **12** (α-D) were isolated in 28% and 27% yield, respectively. Final deprotection of **11** or **12** with Bu_4NF in THF furnished the nucleosides **3** and **4** (*Scheme*). The anomeric configuration of compounds **3**, **4**, **11**, and **12** was assigned from the ^{1}H- and ^{13}C-NMR spectra (*Tables 1* and *2*, resp.)

The ^{1}H-NMR spectra of the β-D-anomers **3** and **11** show a shift of the H–C(2′) and H–C(4′) resonances to a higher field compared to the α-D-anomers **4** and **12** (*Table 1*). Regarding the ^{13}C-NMR spectra, the C(1′) and C(2′) resonances are shifted downfield (4–5 ppm) passing from the β-D-anomers to the α-D-anomers (eclipsing interaction of the base and the F-atom). The same observation can be made with the C(4′) resonances (3–4 ppm). The J(F,C(1′)) coupling constants are decreased by 20 Hz and the J(F,C(2′)) couplings are increased by 6–7 Hz when going from the α-D-anomers **4** and **12** to the β-D-anomers **3** and **11** (*Table 2*). These observations are in good agreement with data previously reported for other pairs of anomers [10]. Moreover, it was stated that the ^5J(H–C(7),F) and ^4J(C(7),F) long-range couplings are observed in the purine 2′-deoxy-2′-fluoro-β-D-arabinofuranonucleosides, but not in the α-D-anomers [10]. These long-range couplings are indicative for the physical proximity of the nuclei involved. In our case, the presence of the ^5J(H–(7),F) and also ^4J(C(7),F) long-range couplings unequivocally characterize the β-D-anomer structures of **3** and **11** (see *Table 2* and *Exper. Part*). In the case of the α-D-anomers **4** and **12**, the assignment of the chemical shifts of C(1′) and C(4′) (which are very close) was made unequivocally from the coupling constants (*Table 2*).

Table 1. *^{1}H-NMR Chemical Shifts and Coupling Constants of Sugar Moieties of Fluorinated Nucleosides*[a])

	δ(H) [ppm]						*J* [Hz]							
	H–C(1′)	H–C(2′)	H–C(3′)	H–C(4′)	H–C(5′)	H′–C(5′)	*J*(1′,2′)	*J*(1′,F)	*J*(2′,3′)	*J*(2′,F)	*J*(3′,4′)	*J*(3′,F)	*J*(4′,5′)	*J*(4′,5″)[b])
3	6.18	5.16	4.36	3.82	3.65	3.59	4.35	13.6	4.4	52.4	4.6	18.4	2.9	4.9
4	6.08	5.42	4.35	4.22	3.55	3.51	2.75	15.8	3.3	51.3	4.75	19.7	4.1	5.3
11	6.22	5.21	4.45	3.97	3.93	3.87	4.4	14.6	*ca.* 3.6	52.1	*ca.* 4.0	18.7	3.5	5.6
12	6.10	5.47	4.51	4.40	3.82	3.78	2.3	16.2	2.5	51.4	4.55	19.9	3.9	5.0

[a]) Measured in (D_6)DMSO. [b]) 5″ is the short form of H′–C(5′).

Table 2. *^{13}C-NMR Chemical Shifts and* J*(F,C)* [Hz] *Coupling Constants of Nucleosides*

	C(2)[c]) C(2)[d])	C(4)[c]) C(6)[d])	C(6)[c]) C(7)[d])	C(7)[c]) C(8)[d])	C(8a)[c]) C(4)[d])	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	C=O (Bz) [i]Bu; [t]Bu
1[a])	149.93	165.34	108.29	115.41	150.25	81.00	95.27	73.21	86.66	60.60	
9/**10**[b])	150.18	161.35	109.69	117.60	150.54	83.01	94.91(**9**) 91.97(**10**)	81.71	84.81	63.62	177.27 35.21; 19.51
3[a])	149.86	165.31	108.25	115.35 (*J* = 3.1)	150.22	80.95 (*J* = 16.65)	95.23 (*J* = 190.9)	71.93 (*J* = 22.9)	83.47 (*J* = 5.75)	60.02	
4[a])	149.95	165.28	108.46	115.04	150.37	85.81 (*J* = 36.0)	99.41 (*J* = 183.95)	73.46 (*J* = 23.15)	86.58 (*J* = 4.5)	60.72	
11[a])	149.78	165.32	108.31	115.14 (*J* = 4.13)	150.36	80.89 (*J* = 16.5)	95.17 (*J* = 190.8)	72.42 (*J* = 23.3)	82.94 (*J* = 5.25)	63.22	26.61; 18.82
12[a])	149.89	165.27	108.49	114.94	150.28	86.26 (*J* = 36.4)	99.37 (*J* = 184.2)	73.19 (*J* = 24.0)	86.23 (*J* = 4.1)	62.85	26.56; 18.85

[a]) Measured in (D_6)DMSO. [b]) Measured in $CDCl_3$. [c]) Systematic numbering. [d]) Purine numbering.

Conformation of the Sugar Moiety. The conformational analysis of the furanose rings of nucleosides **3** and **4** was performed with the PSEUROT program (version 6.3) [24] which calculates the best fits of the three experimental J(H,H) coupling constants ($^3J(1',2'$, $^3J(2',3')$, $^3J(3',4')$) and two experimental J(H,F) coupling constants ($^3J(1',F)$, $^3J(3',F)$) to the five conformational parameters (P (= phase angle of pseudorotation) and ψ_m (= degree of pucker) for both North (N) and South (S) conformers and corresponding mol fractions). The use of both ^3J(H,H) and ^3J(H,F) coupling constants permits a detailed conformational analysis of the pentofuranose rings because of the overwhelming increase of the number of experimental data points over the puckering parameters P and ψ_m [25]. The coupling constants were taken from well-resolved ^{1}H-NMR spectra measured in (D_6)DMSO containing one drop of D_2O. The use of D_2O or (D_6)DMSO alone did not permit to calculate all coupling constants due to signal overlap (*Table 3*). The resulting optimized geometries of *N* and *S* pseudorotamers are presented in *Table 4*.

Table 3. *Pseudorotational Parameters*[a]) *of Compounds* **3**, **4**, *and* **13**–**15**[b]) *and Conformation*[a]) *at the C(4′)–C(5′) Bond of Nucleosides*

	P	$\psi_{m(N)}$	P	$\psi_{m(S)}$	R.m.s.	$\lvert\Delta J_{max}\rvert$	N [%]	S [%]	$\gamma^{(+)g}$ [%]	γ^t [%]	$\gamma^{(-)g}$ [%]
3[c])[d])	– 13.3	36.0[e])	137.6	41.0[e])	0.250	0.76	50	50	58	32	10
4[c])[d])	52.0	34.0[e])	213.1	41.0[e])	0.022	0.08	55	45	40	37	23
13[c])[f])	19.0[e])	36.0[e])	163.5	31.7	0.184	0.300	37	63	48	33	19
14[f])[g])	54.5	41.0[e])	181.0	41.0[e])	0.000	0.000	50	50			
15[f])[g])	19.0	36.0[e])	156.0	36.0[e])	0.400	0.500	29	71	53	30	17

[a]) P = phase angle of pseudorotation, ψ_m = degree of pucker; N = North-type conformation, S = South-type conformation, γ = torsion angle about C(4′)–C(5′). [b]) **13** [26a]: 2-amino-8-(2-deoxy-β-D-*erythro*-pentofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one; **14** [10]: 9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-guanine; **15**: 2′-deoxyguanosine. [c]) Results obtained with three coupling constants. [d]) (D_6)DMSO + εD_2O. [e]) Values fixed during the final calculations. [f]) D_2O. [g]) Results obtained with three coupling constants.

Table 4. *Sugar Conformations of Nucleosides* **3**, **4**, *and* **13**–**18**[a]) *in Solution*

	Conformation		Conformation
3[b])[c])	54% *N*	**14**[d])[e])	50% *N*
4[b])[c])	53% *N*	**15**[d])[e])	29% *N*
13[b])[d])	37% *N*	**17**[b])[c])	98% *N*
16[d])[e])	22% *N*	**18**[d])[e])	37% *N*

[a]) **13** [26a]: 2-amino-8-(2-deoxy-β-D-*erythro*-pentofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one; **14** [10]: 9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)guanine; **15**: 2′-deoxyguanosine; **16** [19]: 2-amino-8-(2-deoxy-α-D-*erythro*-pentofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one; **17** [16]: 6-amino-3-bromo-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one; **18** [26b]: 6-amino-3-bromo-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*- pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one. [b]) Data obtained with five coupling constants. [c]) (D_6)DMSO + D_2O. [d]) D_2O. [e]) Data obtained with three coupling constants.

In the case of the β-D-anomer **3**, the presence of the F-atom shifts the sugar population towards North conformers (54% *N*) in comparison with the 2-amino-8-(2-deoxy-β-D-*erythro*-pentofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one (**13**; 37%) [26a]. The same observation can also be made in the case of 9-(2′-deoxy-2′-fluoro-β-

D-arabinofuranosyl)guanine (**14**; 50% *N*) [10] and 2′-deoxyguanosine (**15**; 29% *N*). Thus, the presence of the F-atom in an 'up' position (*arabino* configuration) enhances the population of the *N* conformers by 21% in the case of guanine nucleosides, and by 17% in the case of 5-aza-7-deazaguanine nucleosides. The *gauche* effect of the ring O-atom and of the F-atom seems to govern the overall sugar conformation. The same behavior was found for the α-D-anomer **4** (53% *N*) compared to 2-amino-8-(2-deoxy-α-D-*erythro*-pentofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one (**16**; 22% *N*) [19]. The conformations at the C(4′)–C(5′) bond of **3** and **4**, taken from the *J*(H,H) coupling constants *J*(4′,5′), and *J*(4′,5″), were calculated according to *Westhof et al.* [27]. The values are similar to that of 2′-deoxyguanosine and 5-aza-7-deaza-2′-deoxyguanosine (**13**) (*Table 3*).

It is known that purine 2′-deoxy-2′-fluoro-β-D-arabinonucleosides exist in a *ca.* 1:1 mixture of *N* and *S* conformers [15]. The strong *gauche* effect of the highly electronegative F-atom leads to a high population of *S* conformers, but in terms of the anomeric effect, the *N* conformer is energetically favored. These different contributions lead to an almost equal population of conformers. This is also observed in our case. The sugar moiety of the β-D-fluoroarabinofuranoside **3** exists to 54% in the *N* conformation, a value which is comparable with that of compound **14** (50% *N*) [10].

Conclusion. – Even if it is known from purine 2′-fluororibonucleosides that the main sugar conformation is the North conformation [28], the situation is more complex for nucleosides with modified nucleobases [16][29]. Examples taken from the literature show normally a preferential South conformation in the case of 2′-fluoro 'up' arabinonucleosides [30]. However, from this study and from our recent findings [16], it is obvious that 2′-fluoro substituents in *arabino* configuration can also lead to sugar moieties with a preferential North conformation. The fluoronucleoside derivatives **3** and **4** were also evaluated *in vitro* for their activity against RNA virus (human immunodeficiency virus, HIV-I) and DNA viruses (BVDV, yellow fever virus YFV, Dengue virus (DENV-I), and West Nile virus (WNV)). No significant antiviral activity was observed.

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Experimental Part

General. Chemicals were purchased from *ACROS*, *Fluka*, or *Sigma-Aldrich*. The 1,3,5-tri-*O*-benzoyl-2-deoxy-2-fluoro-α-D-arabinofuranose (**7**) was a commercial product of *ICN Biomedicals GmbH*. Solvents: technical grade, distilled before use. Eluents (*v*/*v*) for TLC and chromatography: CH_2Cl_2/MeOH 98:2 (*A*), CH_2Cl_2/MeOH 95:5 (*B*), CH_2Cl_2/MeOH 9:1 (*C*), and CH_2Cl_2/MeOH 8:2 (*D*). Flash chromatography (FC): 0.4 bar, silica gel *60 H* (*Merck*, Darmstadt, Germany). TLC: aluminium sheet, silica gel *60* F_{254} (0.2 mm, *VWR*, Germany). M.p: *Berl* block apparatus; uncorrected. UV Spectra: *UV-3000* spectrophotometer (*Hitachi*, Japan); in nm. NMR Spectra: *Bruker-AMX-500* NMR spectrometer at 303 K and at 500.13 MHz for ^{1}H, 125.13 MHz for ^{13}C, and 235.36 MHz for ^{19}F; chemical shift values δ in ppm rel. to internal $SiMe_4$ (^{1}H, ^{13}C) or $CFCl_3$ (^{19}F); coupling constants *J* in Hz; ^{1}H-NMR of **3** and **4** in (D_6)DMSO containing one drop of D_2O. Microanalyses were performed by *Mikroanalytisches Labor Beller*, Göttingen, Germany.

*3,5-Di-*O*-benzoyl-2-deoxy-2-fluoro-*α*-*D*-arabinofuranosyl Bromide* (**8**) [21]. To a soln. of 1,3,5-tri-*O*-benzoyl-2-deoxy-2-fluoro-α-D-arabinofuranose (**7**) [21] (1.0 g, 2.15 mmol) in CH_2Cl_2 (5 ml), 30% HBr soln. in

AcOH (1.2 ml) was added. The mixture was stirred at r.t. for 16 h and evaporated. The oily residue was redissolved in CH_2Cl_2 (20 ml), the soln. washed with H_2O (5 ml) and sat. $NaHCO_3$ soln. (5 ml), dried ($MgSO_4$), and evaporated, and the obtained viscous syrup further dried under high vacuum for 18 h at r.t. and used in the next step without purification.

*2-Amino-8-(2-deoxy-2-fluoro-*D*-arabinofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-ones* (**3**/**4**). Compound **6** [19] (100 mg, 0.45 mmol) was dissolved in dry MeCN (12 ml) under gentle warming. After addition of K_2CO_3 (200 mg, 1.45 mmol) and tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1; 20.24 µl, 63.3 µmol), the soln. was stirred for 10 min at r.t. Then, **8** (200 mg, 0.43 mmol) was added, and stirring was continued for 24 h. The insoluble material was filtered off, the filtrate evaporated, and the residue redissolved in sat. NH_3/MeOH (40 ml) and stirred at r.t. for 24 h. The soln. was evaporated, and the residue applied to FC (silica gel, 10 × 6 cm column, *C* and *D*): inseparable anomer mixture **3**/**4** (67.5 mg, 55%). Colorless foam. For data of the separated anomers, see below. Anal. calc. for $C_{10}H_{12}FN_5O_4$ (285.23): C 42.11, H 4.24, N 24.55; found: C 41.96, H 4.14, N 24.38.

*8-(3,5-Di-*O*-benzoyl-2-deoxy-2-fluoro-*D*-arabinofuranosyl)-2-[(2-methyl-1-oxopropyl)amino]imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-ones* (**9**/**10**). To a suspension of **6** [19] (100 mg, 0.45 mmol) in dry MeCN (5 ml) under Ar was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 70 µl, 0.47 mmol) while stirring at r.t. Stirring was continued for 15 min. A soln. of **8** (200 mg, 0.43 mmol) in MeCN (1.5 ml) was added dropwise (5 min) to the mixture. Stirring was continued for 24 h at r.t. The solvent was evaporated, affording a syrup which was dissolved in eluent *A*, adsorbed on silica gel, and applied to FC (silica gel, 15 × 6 cm column, *A* and *B*): **9**/**10** (170 mg, 70%). Colorless foam. TLC (silica gel, *B*): R_f 0.60. UV (MeOH): 258 (13900). ^{1}H-NMR ($CDCl_3$): 1.23, 1.24, 1.26, 1.27 (4*s*, 12 H, 4 Me); 3.06 ('*sept.*', *J* = 13.49, 26.97, 2 H, CH); 4.82 (*m*, 6 H, H–C(4′)(α/β), H–C(5′)(α/β), H′–C(5′)(α/β)); 5.42 (*m*, 1 H, H–C(2′)(β)); 5.62, 5.70, 5.77 (3*m*, 3 H, H–C(3′)(α/β), H–C(2′)(α)); 6.61 (*m*, 1 H, H–C(1′)(α)); 6.70 (*m*, 1 H, H–C(1′)(β)); 7.45–7.56 (2*m*, 16 H, H–C(6)(α/β), H–C(7)(α/β), Ph); 8.09 (*m*, 8 H, Ph); 8.47 (*s*, 2 H, NH).

*2-Amino-8-(2-deoxy-2-fluoro-*D*-arabinofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-ones* (**3**/**4**) *from* **9**/**10**. The anomeric mixture **9**/**10** (150 mg, 0.27 mmol) was stirred in sat. NH_3/MeOH (7 ml) at r.t. for 24 h. The soln. was evaporated, and the crude product was applied to FC (silica gel, 10 × 6 cm column, *C* and *D*): inseparable anomer mixture **3**/**4** (70 mg, 92%). Colorless foam.

*2-Amino-8-[2-deoxy-5-*O*-{(1,1-dimethylethyl)diphenylsilyl}-2-fluoro-β-*D*-arabinofuranosyl]imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one* (**11**) *and 2-Amino-8-[2-deoxy-5-*O*-{(1,1-dimethylethyl)diphenylsilyl}-2-fluoro-α-*D*-arabinofuranosyl]imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one* (**12**). The anomer mixture **3**/**4** (*ca.* 1:1; 235 mg, 0.83 mmol) in dry DMF (5 ml) was treated with (*tert*-butyl)chlorodiphenylsilane (0.25 ml, 0.96 mmol) and 1*H*-imidazole (140 mg, 2.06 mmol) at r.t. while stirring. Stirring was continued for 48 h, and the solvent was evaporated. The residue was applied to FC (silica gel, 20 × 6 cm column, *B* and *C*). From the faster-migrating zone, the α-*D*-anomer **12** (114.5 mg, 27%) was obtained. Colorless crystals from MeOH. M.p. 194–195°. R_f (*D*) 0.54. UV (MeOH): 258 (14500). ^{1}H-NMR ((D$_6$)DMSO): 1.02 (*s*, 3 Me); 3.78, 3.82 (2*dd*, *J*(5′,5″) = 11.5, *J*(4′,5″) = 5.0, *J*(4′,5′) = 3.9, H–C(5′), H′–C(5′)); 4.40 (*dd*, *J*(3′,4′) = 4.55, H–C(4′)); 4.51 (*dq*, *J*(2′,3′) = 2.52, *J*(3′,F) = 19.9, H–C(3′)); 5.47 (*dt*, *J*(1′,2′) = 2.3, *J*(2′,F) = 51.45, H–C(2′)); 6.10 (*m*, *J*(1′,F) = 16.15, OH–C(3′), H–C(1′)); 7.02 (br. *d*, NH_2); 7.40–7.50, 7.64–7.67 (2*m*, 4 H and 8 H, 2 Ph, H–C(6), H–C(7)). ^{19}F-NMR (D$_6$)DMSO, $CFCl_3$): −188.70 (br. *dt*, *J*(2′,F) = 51.45). Anal. calc. for $C_{26}H_{30}FN_5O_4Si$ (523.63): C 59.64, H 5.77, N 13.37; found: C 60.00, H 5.99, N 13.51.

From the slower-migrating zone, the β-*D*-anomer **11** (119 mg, 28%) was obtained. White powder. R_f (*D*) 0.50. UV (MeOH): 258 (14600). ^{1}H-NMR ((D$_6$)DMSO): 1.02 (*s*, 3 Me); 3.87, 3.93 (2*dd*, *J*(5′,5″) = 11.4, *J*(4′,5″) = 5.6, *J*(4′,5′) = 3.5, H–C(5′), H′–(5′)); 3.97 (*m*, *J*(3′,4′) ≈ 4.0, H–C(4′)); 4.45 (*m*, *J*(2′,3′) ≈ 3.6, *J*(3′,F) = 18.7, H–C(3′)); 5.21 (*dt*, *J*(1′,2′) = 4.4, *J*(2′,F) = 52.1, H–C(2′)); 6.08 (*d*, *J* = 4.85, OH–C(3′)); 6.2 (*dd*, *J*(1′,F) = 14.6, H–C(1′)); 7.06 (br. *d*, NH_2); 7.1 (*t*, *J*(7,F) = 2.1, H–C(7)); 7.3 (*d*, *J*(6,7) = 2.4, H–C(6)); 7.40–7.50, 7.63–7.66 (2*m*, 4 H and 6 H, 2 Ph). ^{19}F-NMR (D$_6$)DMSO; $CFCl_3$) −200.06 (br. *dt*, *J*(2′,F) = 52.1). Anal. calc. for $C_{26}H_{30}FN_5O_4Si$ (523.63): C 59.64, H 5.77, N 13.37; found: C 59.93, H 6.01, N 13.24.

*2-Amino-8-(2-deoxy-2-fluoro-β-*D*-arabinofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one* (**3**). To a soln. of **11** (170 mg, 0.33 mmol) in THF (0.8 ml), a soln. of Bu_4NF in THF (1.2 ml) was added while stirring at r.t. for 0.5 h. The soln. was evaporated and applied to FC (silica gel): **3** (88 mg, 95%). Colorless powder. R_f (*D*) 0.59. UV (MeOH): 258 (14700). ^{1}H-NMR ((D$_6$)DMSO): 3.59 (*dd*, *J*(4,5″) = 4.9, *J*(5′,5″) = 12.05, H′–C(5′)); 3.65 (*dd*, *J*(4,5′) = 2.9, H–C(5′)); 3.82 ('*q*', *J*(3,4′) = 4.6, H–C(4′)); 4.36 (*dt*, *J*(2′,3′) = 4.4, *J*(3′,F) = 18.4, H–C(3′)); 5.16 (*dt*, *J*(1′,2′) = 4.35, *J*(2′,3′) = 4.4, *J*(2′,F) = 52.4, H–C(2′)); 6.18 (*dd*, *J*(1′,2) = 4.35, *J*(1′,F) = 13.6, H–C(1′)); 9.25 (*d*, *J*(6,7) = 10.9, H–C(6)); 9.6 (*m*, *J*(6,7) = 10.9, *J*(7,H) = 2.7, H–C(7)). ^{19}F-NMR (D$_6$)DMSO; $CFCl_3$);

– 200.32 (br. *dt*, *J*(1′,F) = 13.6, *J*(2′,F) = 52.4, *J*(3′,F) = 18.4). Anal. calc. for $C_{10}H_{12}FN_5O_4$ (285.23): C 42.11, H 4.24, N 24.55; found: C 42.07, H 4.40; N 24.06.

*2-Amino-8-(2-deoxy-2-fluoro-α-*D*-arabinofuranosyl)imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)-one* (**4**). As described for **3**, with **12** (120 mg, 0.23 mmol): **4** (62 mg, 95%). Colorless powder. R_f (*D*) 0.59. UV (MeOH): 258 (14600). ^{1}H-NMR ((D$_6$)DMSO): 3.51 (*dd*, *J*(4,5″) = 5.3, *J*(5′,5″) = 12.2, H–C(5″)); 3.55 (*dd*, *J*(4,5′) = 4.1, *J*(5′,5″) = 12.2, H–C(5′)); 4.22 (‘*q*’, *J*(3′,4′) = 4.8, H–C(4′)); 4.35 (*m*, *J*(3′,4′) = 4.75, *J*(3′,F) = 19.7, H–C(3′)); 5.42 (*dt*, *J*(2′,3′) = 3.3, *J*(2′,F) = 51.3, H–C(2′)); 6.08 (*dd*, *J*(1′,2′) = 2.8, *J*(1′,F) = 15.8, H–C(1′)); 7.35 (*d*, *J*(6,7) = 2.7, H–C(6)); 7.40 (*d*, *J*(7,6) = 2.7, H–C(7)). ^{19}F-NMR ((D$_6$)DMSO; $CFCl_3$): – 189.93 (br. *ddd*, *J*(1′,F) = 15.8, *J*(2′,F) = 51.3, *J*(3′,F) = 19.7). Anal. calc. for $C_{10}H_{12}FN_5O_4$ (285,23): C 42.11, H 4.24, N 24.55; found: C 41.86, H 4.34, N 24.14.

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